

# Experiences with Antimicrobial Resistance in DoD Health Care Centers

## The BAMC Experience

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# Antimicrobial Resistance

## Recent Patterns & Anecdotal Reports

- Gram positive cocci
  - Increasing percentage of hospital *S. aureus* isolates are MRSA
  - More virulent, community-acquired MRSA
  - Increasing VRE colonization and infection
  - Resistance to newer agents - linezolid
  - Resistance to older agents - vancomycin



# Antimicrobial Resistance

## Recent Patterns & Anecdotal Reports

- Gram negative bacilli (rods)
  - Importation of MDRO *Acinetobacter* from Iraq
  - Increasingly resistant MDRO infections
    - Resurrection of older, more toxic antimicrobial agents



# Drug Resistance at BAMC

## Recent Patterns

- Microbiology tracks recovery of "reportable agents"
- Infection Control tracks colonization and infection with selected "problem agents"



# Drug Resistance at BAMC

## Recent Patterns

	1999	2000	2001	2002	2003	2004
<b><i>Acinetobacter</i></b>	--	--	--	1	10	37 (46)
<b><i>Citrobacter</i></b>	--	--	--	--	--	1 (1)
<b><i>Enterobacter</i></b>	--	--	--	--	--	5 (6)
<b><i>E. Coli</i></b>	--	--	--	--	1	0 (0)
<b><i>Klebsiella</i></b>	--	--	--	--	2	7 (9)
<b><i>Pseudomonas</i></b>	--	--	--	--	17	18 (23)
<b>MRSA</b>	96	91	117	173	232	209 (261)
<b>VRE</b>	7	11	11	17	9	4 (5)



# Gram Positive Cocci

## The BAMC Experience

- Nosocomial MRSA
- Community-acquired MRSA
- VRE



# Methicillin-resistant *Staphylococcus aureus*

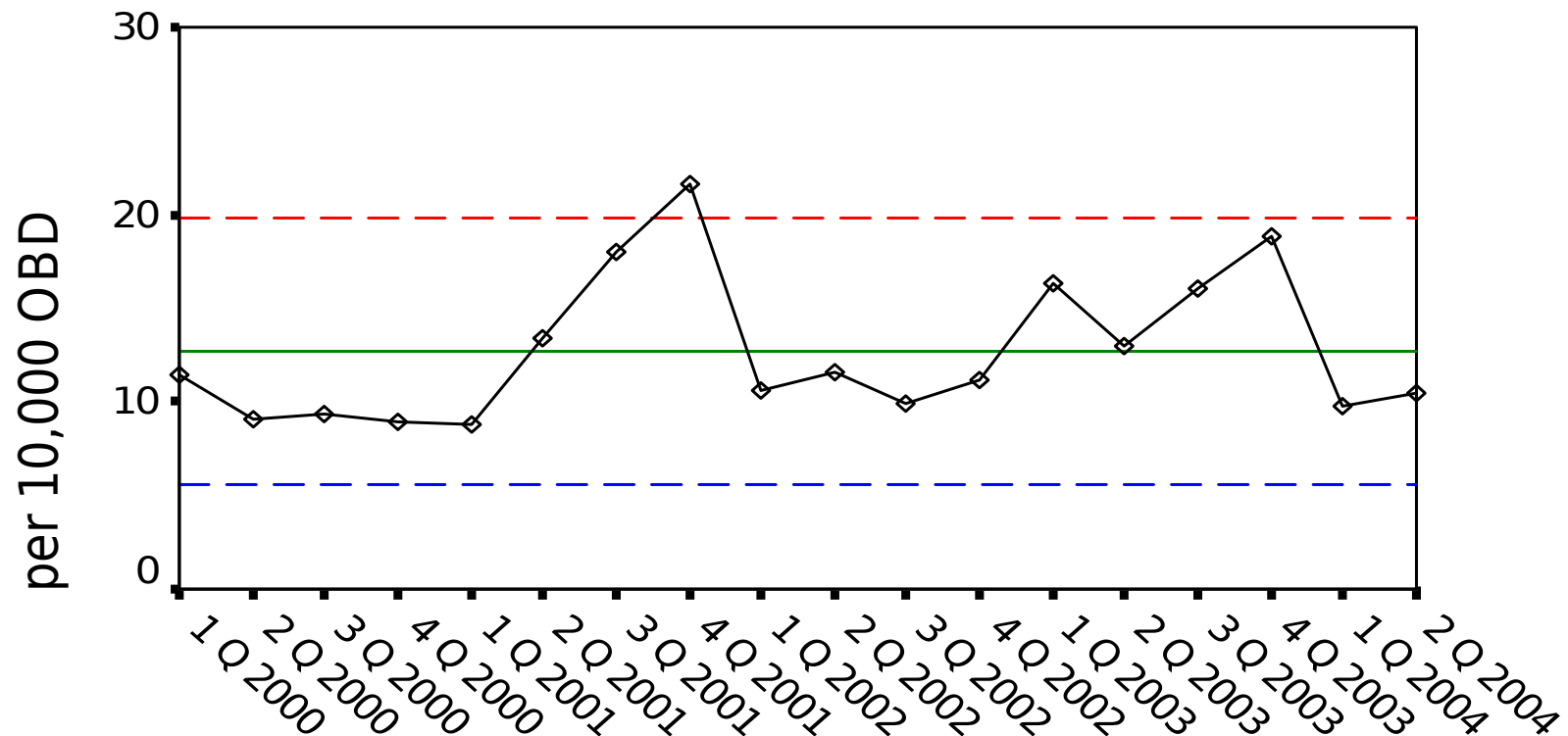
Nosocomial MRSA



# Nosocomial MRSA

Less Surveillance cultures 2Qtr 2004

2000-2004



Sigma level: 2



# Methicillin-resistant *Staphylococcus aureus*

Community-acquired MRSA



# Community-acquired MRSA

## Changing/emerging epidemiology

- Penicillin resistance reported in 1940s
- Methicillin resistance reported in 1960s
  - Unique penicillin-binding protein, PBP 2'
  - 1968, first US hospital outbreak
  - MRSA in ICUs becomes commonplace
  - Generally not an outpatient issue



# Community-acquired MRSA

## Changing/emerging epidemiology

- cMRSA, CA-MRSA
- Slow spread until more recently
- Definitions (?)
  - Organism recovered as outpatient or < 48 hours of hospitalization
  - No hospitalization, renal dialysis, surgery, IV therapy, long-term care facility stay in the previous year
  - No history of IVDU, prior MRSA infection or colonization



# Community-acquired MRSA

## Changing/emerging epidemiology

- Increasing reports of cMRSA skin and soft tissue infection in children, high school (and other) sports participants, jail prisoners, other groups
- Rare reports of cMRSA producing sepsis in children
- Recent studies have documented increased rates and more virulent strains



# Community-acquired MRSA

## Resistance & Virulence

- PBP 2' (cMRSA) - SCC*mec* type IV gene
  - Gene cassette, smaller than other *mec*
  - No other antimicrobial resistance genes
- cMRSA may have susceptibility to other common antimicrobials
  - Often sensitive to TMP/SMX, tetracyclines
  - Some sensitive to fluoroquinolones, macrolides, clindamycin (beware erythro resist/clinda sens)
- Virulence genes appear common
  - Enterotoxin H, Panton-Valentine leukocidin (PVL)



# Community-acquired MRSA

## Resistance & Virulence

- Panton-Valentine leukocin (PVL)
  - Temperate phage
  - Most cMRSA
  - Associated with more severe skin and soft tissue infections and necrotizing pneumonia
  - Lyses leukocytes
  - Causes dermolysis in experimental animals
  - Appears to be associated with bacterial "fitness"



# Community-acquired MRSA

## Recent BAMC Research - Inpatient

- Natural history of those colonization with MRSA at hospital admission (cMRSA?)
- N=758 admitted to 5 select units
- One-year follow up
- MRSA colonization - 3.4% (MSSA - 20%)
- MRSA infection
  - **MRSA colonized - 19%**
  - MSSA colonized - 1.5%
  - Non-colonized - 1.6%

Clin Infect Dis  
2004;39:776



# Community-acquired MRSA

## Recent BAMC Research - Outpatient

- Natural history of cMRSA colonized combat medic (91W) trainees
- N=812 healthy volunteers
- Initial nares colonization
  - cMRSA 3%, cMSSA 28%
- 8-10 wk nares colonization
  - cMRSA 1.6%, cMSSA 20%
- Skin and soft tissue infections
  - **cMRSA colonized 38%**, cMSSA colonized 3%

Clin Infect Dis  
2004;39:971





# Community-acquired MRSA

## Recent BAMC Research - Outpatient

- PVL genes were detected in 66% of cMRSA
- PVL genes were detected in **all recovered infection-causing isolates** (and a bacteremic isolate of a non-participant hospitalized with cellulitis)

Clin Infect Dis  
2004;39:971



# Vancomycin-resistant *Enterococcus* species

Nosocomial VRE



# Vancomycin-resistant *Enterococcus*

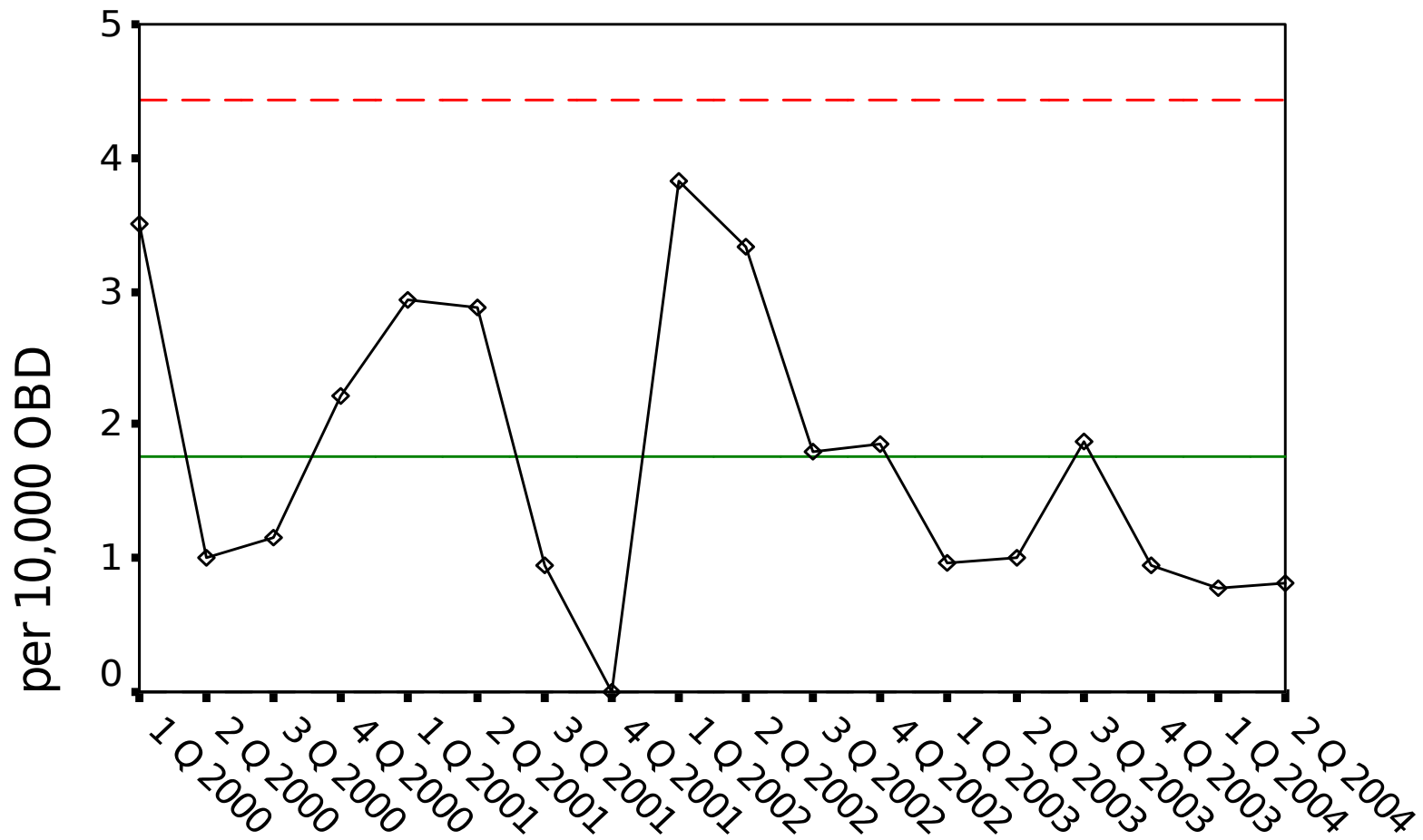
## Nosocomial Infections at BAMC

- Uncommon at BAMC
  - Level I trauma center
  - No solid or stem cell transplantation



# Nosocomial VRE

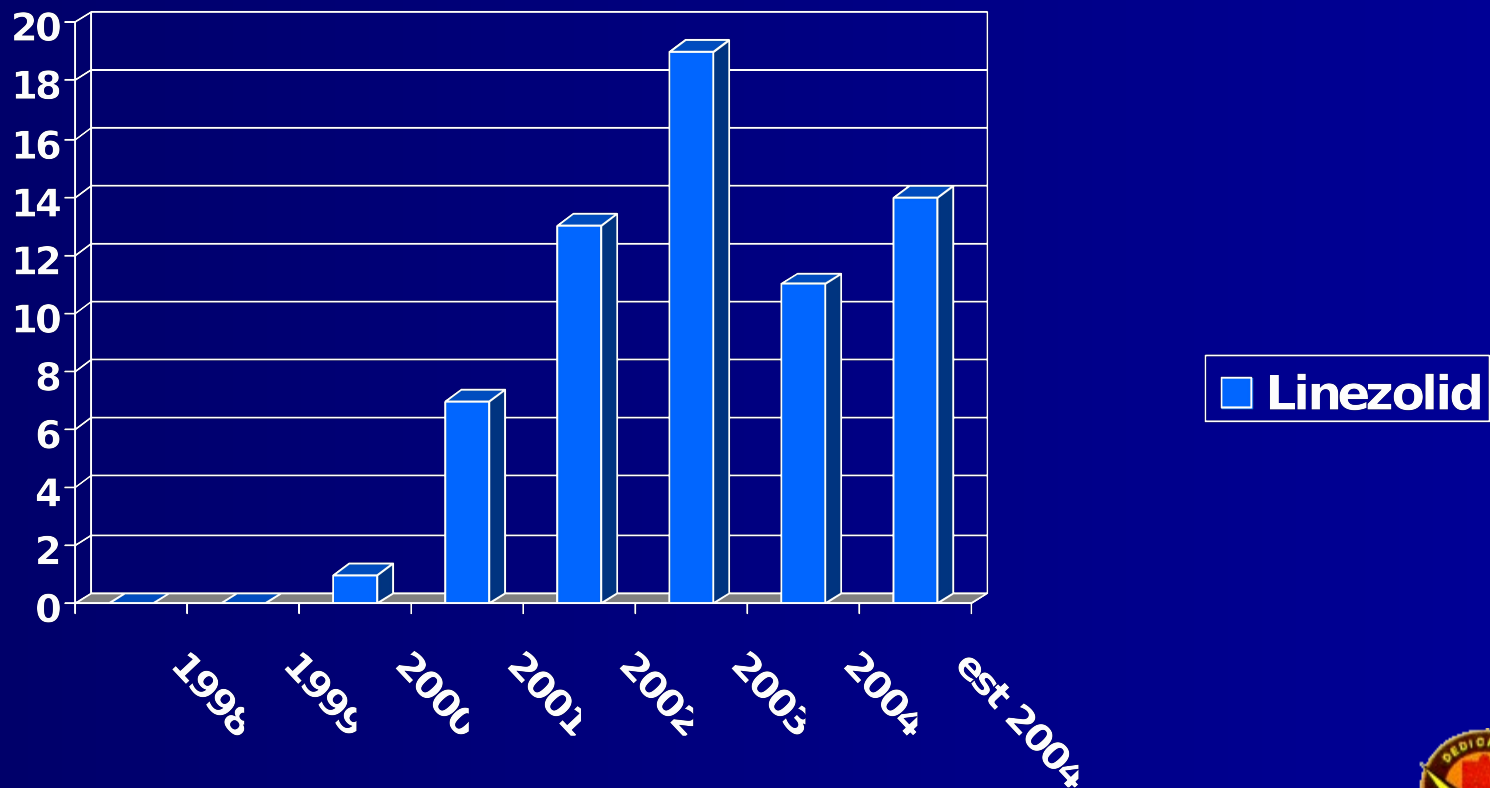
2000-2004



Sigma level: 2

# Vancomycin-resistant *Enterococcus*

## Nosocomial Infections at BAMC



# Multidrug-resistant Organisms (MDRO)



# Multidrug Resistant Organisms

## Definitions

- Bacteria resistant to at least one class of antimicrobials
- Susceptible to 2 or less commonly used antimicrobials
- MDRO is usually used to describe multidrug resistant aerobic gram negative bacilli (GNRs)



# Multidrug Resistant Organisms

## Definitions

- Definitions imperfect
  - Based on which Vitek card used/antimicrobials tested at any particular institution
  - Reporting does not identify "how resistant"
    - Antimicrobial class v. individual drug
    - Total number of drugs resistant to and/or total number tested against





# Multidrug Resistant Organisms

## Recovery at BAMC

	1999	2000	2001	2002	2003	2004
<b><i>Acinetobacter</i></b>	--	--	--	<b>1</b>	<b>10</b>	<b>37 (46)</b>
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# Multidrug-resistant Organisms (MDRO)

*Acinetobacter* species



# Multidrug Resistant Organisms

## *Acinetobacter* at BAMC

- Canary in the coal mine?
- Nosocomial *Acinetobacter* has been around a while
  - Common on personnel, tracheostomy sites
  - NNIS data - 0.6% of hospital-acquired infection, 3% of hospital-acquired pneumonias
  - Most common gram negative contaminating traumatic extremity injuries in Vietnam conflict



# MDR *Acinetobacter* Infections

## Operation Iraqi Freedom (OIF)

- USNS Comfort

- First noted colonization/wound infections
- Onset of OIF
- 1/3 of wound cultures
- 1/4 of all WIA



# MDR *Acinetobacter* Infections

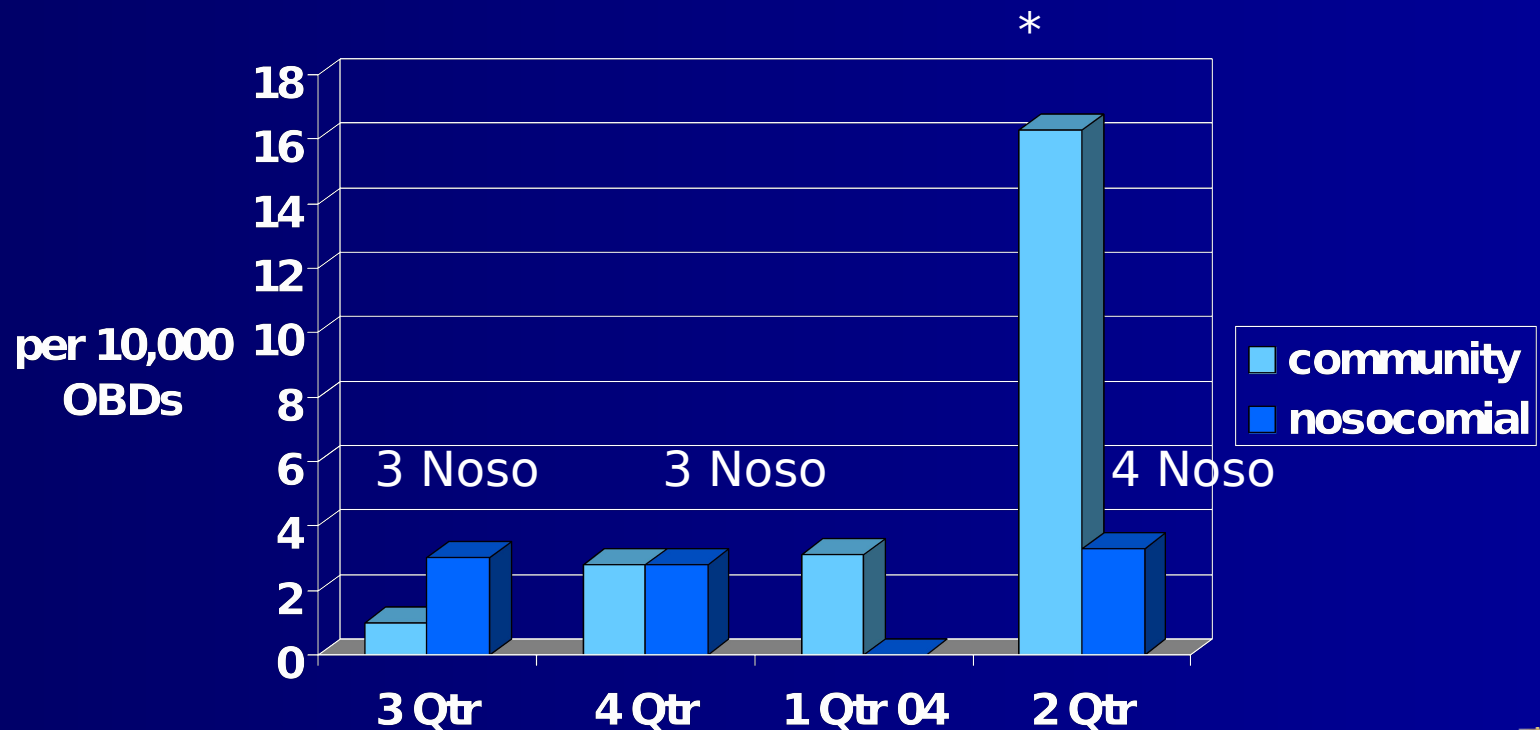
## Operation Iraqi Freedom (OIF)

- Colonization/wound infections
  - Up to June 2004
  - ~350 patients with positive cultures
  - ~200 patients with infections
  - Most infections in wounds from major traumatic injuries



# Multidrug Resistant Organisms

## *Acinetobacter* at BAMC



\* Started actively performing surveillance cultures



# MDR *Acinetobacter* Infections

## BAMC GWOT Experience

Active duty service personnel admitted for injuries

	Dec02 - Feb03	Mar03 - May04
<i>Acinetobacter</i> positive cultures	0%	70% (n=56)
Other positive cultures	100%	30% (n=24)



# MDR *Acinetobacter* Infections

## BAMC GWOT Experience

- *Acinetobacter* positive
- Injured, active duty, n=56
- 61% (34) infections
- 39% (22) colonization





# MDR *Acinetobacter* Infections

## BAMC GWOT Experience

Active duty service personnel admitted for injuries

	OIF Exposure	No OIF Exposure
Actual infections	63% (n=30)	50% (n=4)
Probable colonizations	37% (n=18)	50% (n=4)
Cross infections	0	2



# MDR *Acinetobacter* Infections

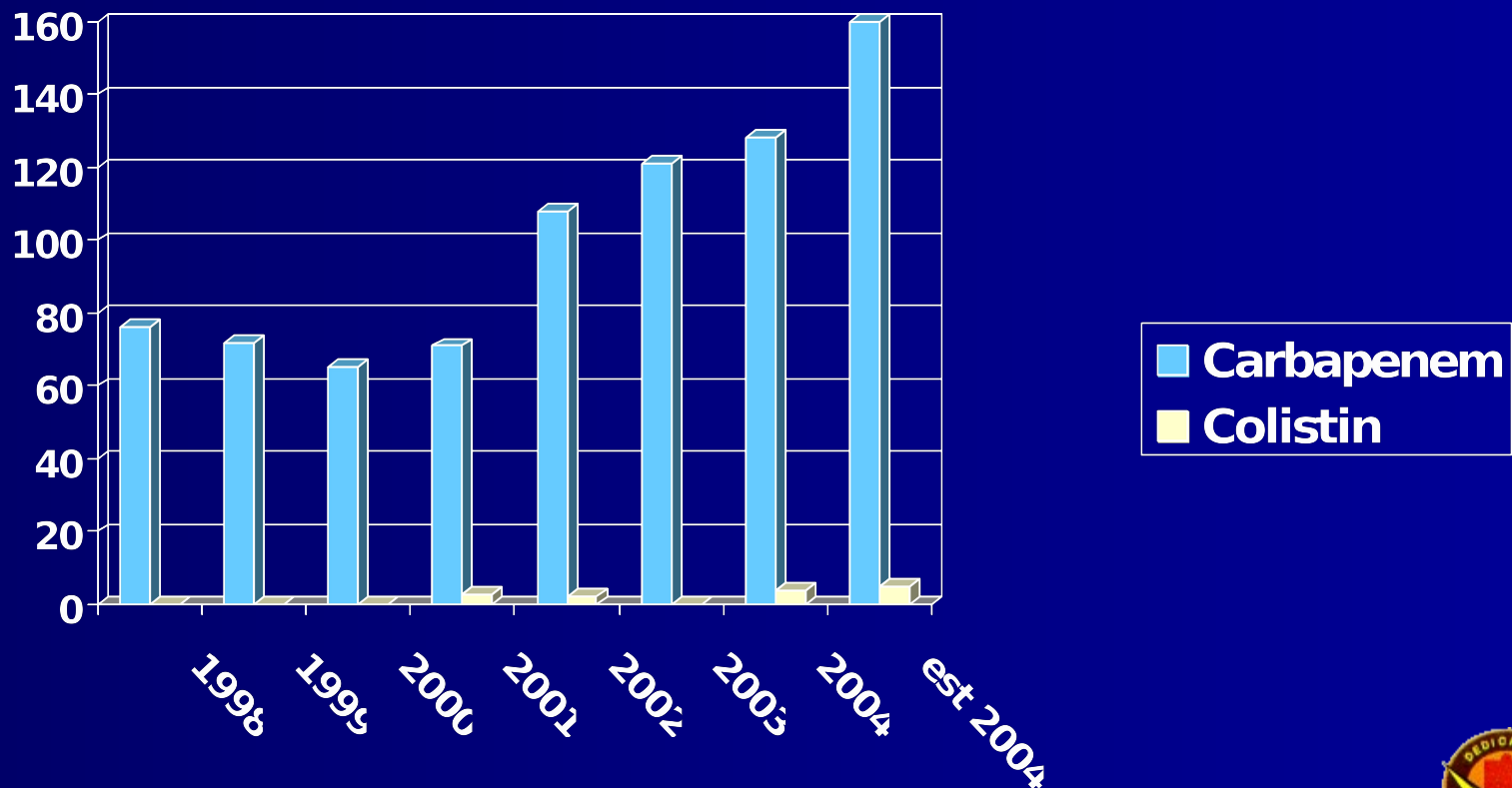
## OIF Resistance Patterns

- *A. baumannii* OIF isolates
  - Most remain sensitive to imipenem/cilastatin
  - Many are sensitive to amikacin as well (~1/4)
  - Two have been found to be resistant to all tested antimicrobials (not BAMC)



# Multidrug Resistant Organisms

## Antimicrobial Usage at BAMC



# Multidrug-resistant Organisms (MDRO)

Other GNRs



# Multidrug Resistant Organisms

## Infections at BAMC

- Other MDRO GNR data less ideal
- Infection Control tracking only recently started
- Microbiology data base is available



# Multidrug Resistant Organisms

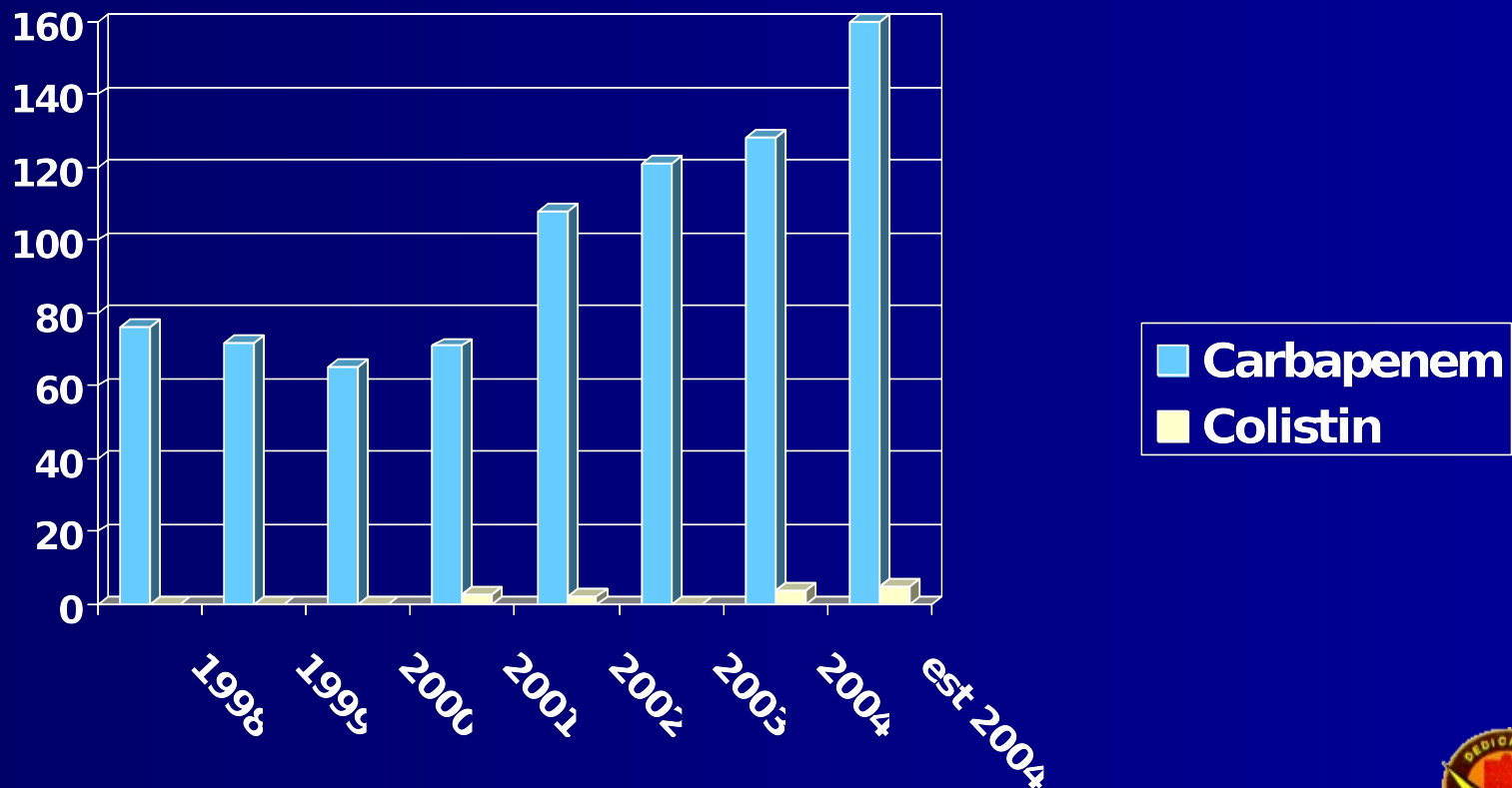
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# Multidrug Resistant Organisms

## Antimicrobial Usage at BAMC



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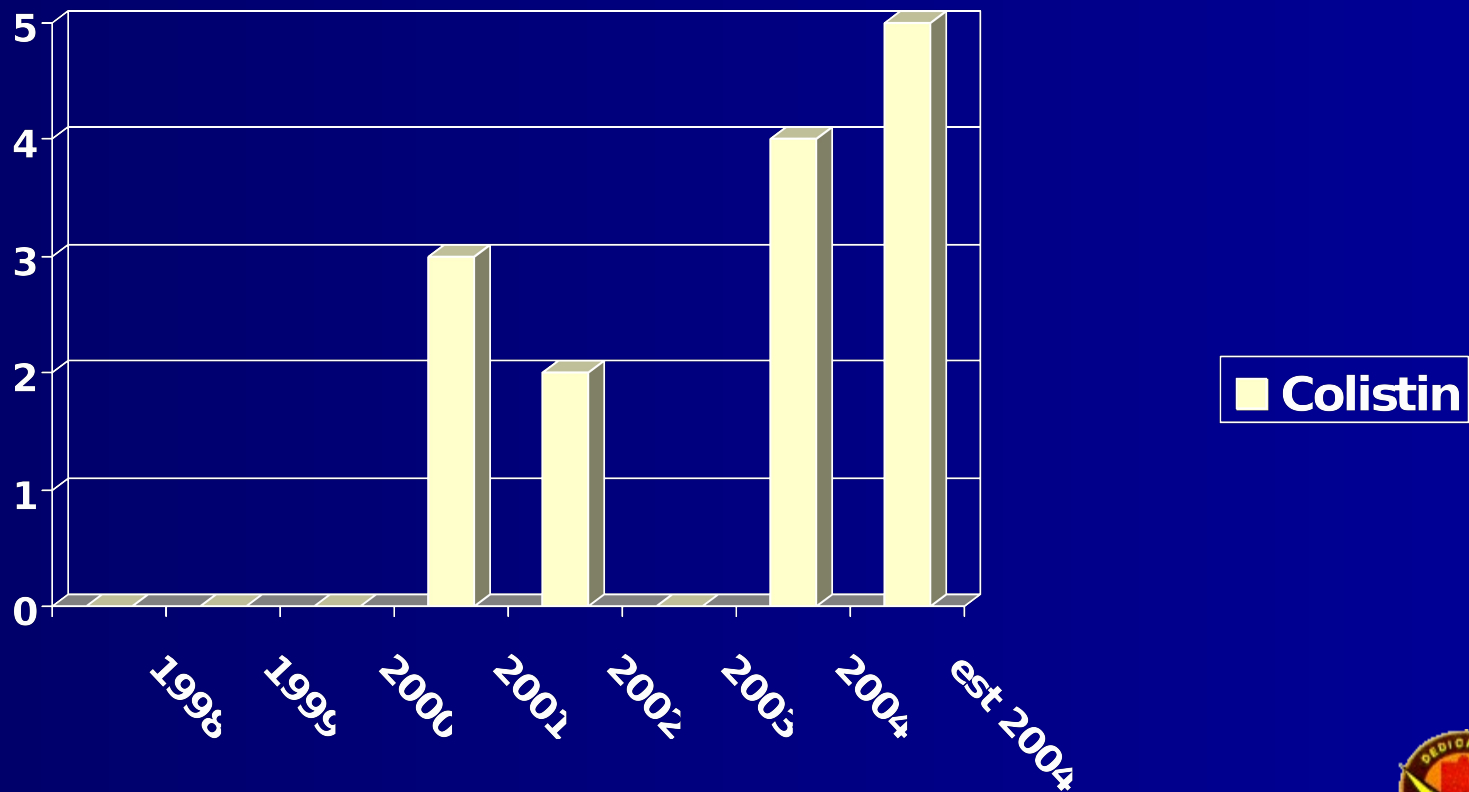
- Virtually no GNR drugs in the pipeline
- Back to the future?
- Polymyxin B and E (colistin)
  - Renal toxicity (ATN) - 20-25% significant toxicity
  - Neurotoxicity





# Multidrug Resistant Organisms

## Antimicrobial Usage at BAMC



# Multidrug Resistant Organisms

## Antimicrobial Usage at BAMC

- What about when we run out of drugs?
- Anecdotal - one trauma patient "ran out" this last year
- No known BAMC deaths . . . yet
- JCAHO Sentinel Events mandate



# Antimicrobial Resistance in DoD

## The BAMC Experience

- Do we need new antimicrobial agents - YES
- Are we adequately tracking the problem with nosocomial MDRO GNRs - NO



# BAD BUGS, No DRUGS

As Antibiotic Discovery Stagnates ...  
A Public Health Crisis Brews



**IDSA**

Infectious Diseases Society of America



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